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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/327,761	06/07/1999	DONALD W. PETERSEN	99.501	5876

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EXAMINER
WITZ, JEAN C

ART UNIT	PAPER NUMBER
1651	26

DATE MAILED: 09/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/327,761	PETERSEN ET AL.	
	Examiner	Art Unit	
	Jean C. Witz	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,12-21 and 35-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,12-21 and 35-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 23 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 25, 2003 has been entered.

Response to Arguments

Applicant's arguments filed August 26, 2003 have been fully considered but they are not persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-3, 12-21 and 35-38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of O'Leary et al. (5,484,601), Yim et al. (5,385,887) and Gertzman et al. (6,030,635) taken as a whole for the reasons of record.

Applicants argue that Gertzman teaches away from the use of calcium sulfate in a bone graft composition by pointing to the disclosure of Gertzman at col. 1, lines 42-47, which Applicants allege that state that the calcium sulfate is "bioinert and [does] not absorb or become remodeled into natural bone" and that it remains "in place indefinitely as a brittle, foreign body in the patient's tissue."

With regard to the Gertzman et al. teaching discussed by Applicants, this issue was addressed in the previous office action. In the previous office action, the Examiner noted that Gertzman's assertion regarding calcium sulfate is not supported by the state of the art regarding the use of calcium sulfate in bone implants. The disclosures cited not as prior art but instead to show the state of the art of calcium sulfate hemihydrate used as in vivo implants included the disclosures of Sidqui et al. (the abstract), Ricci et al. ('636 - paragraph 0003), Ricci et al. ('206 – col. 5, lines 21-22), Randolph et al. ('567 – col. 1, lines 10-25), Grisoni et al. ('127 – col 1, lines 20-27), Snyders, Jr. ('769 – col. 3, lines 3-6). Applicants' position that these references are "phantom art" are strenuously objected to and not well taken. Applicants' own quote states that the Board found that the Examiner in the Stern case failed to articulate "any recognizable theory" to support the rejection, and that the Board requires "the requisite factual basis". The Examiner in this case has provided the requisite factual basis to rebut Applicants' reliance on the statements of Gertzman. The Examiner has made these references of record so that their basis for rebuttal can be reviewed; however, since they are being used solely to rebut Applicants' assertion regarding the teaching of the Gertzman patent, they are not necessary to the basis of the rejection. If Applicants choose to rely upon an incorrect

or confusing statement in the Gertzman patent for the basis of their arguments, this is Applicants' prerogative. However, the Examiner has provided overwhelming evidence that the statement of Gertzman is either incorrect or taken out of context, as indicated below.

As evidenced by the disclosure of the seminal patent by Hanker et al. in the art of the use of calcium sulfate hemihydrate as a bone implant material (U.S. 4,619,655 – cited as evidence of that which is well known in the art and not as a new reference in the rejection), calcium sulfate (or plaster of paris) "is totally resorbed within a few weeks, being replaced initially by fibrous connective tissue." The fibrous connective tissue "becomes incorporated into new bone." See col. 3, lines 5-15. At col. 5, lines 1-5, the calcium sulfate is described as being "rather rapidly resorbed and replaced by connective tissues, and elicits no immunologic or inflammatory response." U.S. Patent 6,030,636, to Randolph et al. (filed after the filing date of the Gertzman patent and issued on the same date as the Gertzman patent and cited as evidence of that which is well known in the art and not as a new reference in the rejection) similarly teaches that "Calcium sulfate has been utilized as a filler for bone cavities . . ." and "it is biocompatible and is progressively resorbed by the body."

It is noted that immediately prior to the reference to calcium sulfate, the Gertzman patent states "These inorganic materials include hydroxyapatite obtained from sea coral or derived synthetically." It can only be surmised that perhaps Gertzman, when stating "These inorganic materials are osteoconductive but are bioinert and do not absorb or become remodeled into natural bone. They consequently remain

in place indefinitely as a brittle, foreign body in the patient's tissue", was referring to hydroxyapatite, which per the disclosure of Hanker et al., agrees with Gertzman regarding the lack of resorption of hydroxyapatite when implanted in the human body, and the reference to calcium sulfate and plaster of paris was inadvertently placed in the center of this paragraph.

Further, Applicants' arguments the Gertzman teaches that demineralized bone was a good alternative to calcium sulfate is not persuasive. First, the objects the invention of Gertzman address an improvement in the hydrogel formulation of a known bone implant material, demineralized bone. Gertzman fails to explicitly state that demineralized bone is included as an alternative to calcium sulfate. Second, since it is clear that demineralized bone matrix, as its name indicated, contains no inorganic components and therefore no calcium salts. Therefore, it remains unclear how Applicants can conclude that Gertzman would consider two components known to have been included in prior art bone graft compositions but completely different in composition as alternatives to one another in either composition or effect. In fact, Gertzman suggests that calcium salts be included "to aid in the healing in the bone defect site." See col. 4, lines 35-40.

Applicants fail to address the importance of the Gertzman reference to the rejection as stated in Paper #15. The patent to Gertzman shows that malleable pastes are preferred in treating bone defects and that numerous substances are well known to be included in compositions for treating bone defects such as autologous bone, allograft bone, bone marrow and blood.

With regard to the O'Leary patent, Applicants continue to argue that the term "inorganic elements" disclosed in the O'Leary patent do not and cannot be referring to calcium salts such as calcium sulfate. As stated in the previous office action, the Examiner acknowledges that the disclosure of O'Leary does not explicitly disclose the inclusion of calcium sulfate; however, O'Leary teaches that "any variety of substances" may be included in the composition, including what O'Leary describes as "inorganic elements." Applicants again assert that the Examiner has taken this disclosure of O'Leary out of context, describing the Examiner's interpretation of the "inorganic elements" disclosure of O'Leary to include calcium salts such as calcium sulfate as "hindsight" and and again argue that the inorganic elements of O'Leary should be limited to components that "have a biological function or be bioactive."

As stated previously, such an interpretation of O'Leary is too narrow. Terms in both specifications, claims and in the prior art patents are given their broadest reasonable interpretation consistent with the specification. There is nothing in the O'Leary specification that specifically states that calcium salts and specifically calcium sulfate is not intended to be included. In fact, since the composition of O'Leary is specifically designed to be implanted for bone repair and since bone tissue is composed to a great degree of inorganic elements such as calcium, it would be expected that broadest reasonable interpretation of the term "inorganic elements" included sources of calcium. Further, it remains unclear how the inorganic elements of O'Leary would be expected to have a bioactive effect yet the calcium sulfate, clearly inorganic, would not have a similar bioactive effect. Bone is composed of both organic and inorganic

components and calcium is deposited in inorganic form in bone tissue to provide a hardening effect to the bone tissue so that the bone tissue can provide the required support for the organism. It is not seen how this effect is anything other than bioactive. Also, at the time the invention was made, one of ordinary skill in the art would have been aware that the calcium sulfate hemihydrate would eventually be resorbed, and the calcium contained therein would be used to replace the calcium sulfate hemihydrate with bone tissue. Again, it remains unclear how this effect is not "bioactive".

Finally, Applicants appear to assert that the addition of the calcium sulfate to the composition of O'Leary would not cause the calcium sulfate to harden due to the polyol nature of the O'Leary composition. However, this is not necessarily a detriment to the composition of O'Leary. This will ensure the workability of the composition until it is implanted into the body. Then the aqueous nature of the body fluid, including blood at the implant site, will activate the calcium sulfate hemihydrate, causing it to harden in situ.

Applicants continue when addressing the Yim reference to assert that Gertzman teaches that demineralized bone is a better carrier than calcum sulfate. As discussed above, the Examiner finds no basis for this assertion in the disclosure of Gertzman as addressed above. Applicants also continue to argue that there would be no motivation to either use demineralized bone in the composition of Yim or to add the calcium sulfate to the composition of O'Leary. Such an argument does not take into consideration the concept of "reduced set-up time" discussed by Yim as a benefit of the inclusion of the calcium sulfate hemihydrate. It is clear that regardless of the "putty-like" nature of a

composition prior to its implantation in vivo, upon implantation, said composition comes in contact with physiological fluids in varying amounts dependent upon the condition to be treated and these fluids can act to both dilute and dissolve components of the composition such that the composition may not be fully retained at the wound site. Yim teaches (at col. 7, beginning at line 50) that the calcium sulfate hemihydrate improves "retention of the formulation at the wound site." This is not an issue of the consistency of the formulation prior to implantation; instead, Yim provides motivation to include the calcium sulfate hemihydrate to improve retention of the formulation upon implantation at the wound site due to the known and expected hardening abilities of the calcium sulfate hemihydrate when hydrated. Therefore, it is not seen to be redundant to include the calcium sulfate hemihydrate in the composition of O'Leary.

With regard to claims 3 and 20, claim 3 requires about 40% demineralized bone matrix by weight and claim 20 requires about 69.4 parts demineralized bone matrix by weight (about 20%), as well as 100 parts calcium sulfate hemihydrate (about 30%), 11.1 parts carboxymethylcellulose by weight (about 3%) and about 162 parts water by weight (about 47%). Applicants assert that "the use of these specific quantities is not suggested anywhere in Gertzman, O'Leary or Yim."

However, O'Leary teaches that the demineralized bone powder is included in amounts from about 5 to 80 weight percent and preferably 20 to 60 weight percent, within which the 40% of claim 3 and the 20% of claim 20 clearly fall. Yim et al. teaches that the cellulosic component is included in amounts from 2 to 10% weight by volume.

Therefore, the amounts claimed are clearly disclosed as conventional in the formulation of bone implant compositions.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (703) 308-3073. The examiner can normally be reached on 6:30 a.m. to 4:00 p.m. M-Th and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (703) 308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jean C. Witz
Primary Examiner
Art Unit 1651

September 2, 2003